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REMARKS

Claims 1-40 are pending in the present application.

The rejection of Claims 1, 2, 10, and 15 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

Claims 1 and 2 have been rewritten to clarify the relationship between the parent sequence and the claimed mutation.

Applicants wish to make specific note of an error in original Claims 1 and 2, as well as the specification at page 3, line 14 and page 6, line 3 (originally submitted specification designation). At these sections, the mutation at position 369 of SEQ ID NO:1 and positions corresponding thereto appeared as D369D. Applicants submit that this is an obvious error since there must be an actual change in the amino acid to be a "mutant." The claims and the specification at page 3, line 14 and page 6, line 3 should properly indicate the mutation as D369N. Support for this correction appears on page 10, lines 20-23 and Table 2 on page 30. Applicants submit that the amendment to the specification and to Claims 1 and 2 do not constitute new matter.

In view of the amendment presented herein, Applicants submit that Claim 1 and all claims dependent therefrom, including Claim 10, as well as Claim 2 and all claims dependent therefrom, including Claim 15, are definite. Applicants request withdrawal of this ground of rejection.

The rejection of Claims 1, 2, 10, and 15 under 35 U.S.C. § 112, first paragraph ("written description") is obviated in part by amendment and traversed in part.

The Office has alleged that the specification fails to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (paper number 15, paragraph bridging pages 10 and 11). Specifically, the Office has alleged that the specification fails to provide an adequate number of representative species to support the genus provided in the present claims (paper number 15, paragraph bridging pages 10 and 11). Applicants respectfully disagree.

It appears that this ground of rejection is based on the breadth of the claims in so much as the claims as previously presented lacked a recitation of the parent sequence (Claim 1) or provides a genus defined by 60% homology with SEQ ID NO:1.

MPEP § 2163.02:

> An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

The Office asserts that "the specification teaches the structure of only a single representative species of such polypeptides, SEQ ID NO:1. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding an alkaline protease." (paper number 15, paragraph bridging pages 10 and 11).

At the outset, Applicants have amended Claim 1 to define the parent sequence as being SEQ ID NO:1, which the Examiner has conceded as being adequately described. Therefore, the Examiner has already conceded compliance with the written description requirement for this claim and the claims dependent therefrom.

Turning to Claim 2, Applicants have amended this claim to limit the scope of the claimed homologs to 80% of SEQ ID NO:1 for the regions outside of the claimed,

alternative, mutation sites and to specifically require that the alkaline proteases within the scope of this claim have oxidant resistance, are active at an alkaline pH, and retain at least 80% residual activity when treated at pH 10 for 10 minutes.

To this end, Applicants note that the assertion by the Examiner that "the specification teaches the structure of only a single representative species of such polypeptides, SEQ ID NO:1" is incorrect. Specifically, the Examiner's attention is directed to the disclosure at page 8, line 13 to page 9, line 13 (original specification designation), which clearly provides a total of 7 examples (SEQ ID NOs: 1-7) of "such polypeptides."

With respect to the phrase "a position corresponding thereto," the Examiner's attention is directed to the specification at page 9, line 14 to page 13, line 20 (original specification designation). In this section of the specification the artisan is explicitly directed as to how one would identify the position corresponding to the claimed mutation points by use of the Lipman-Pearson method (Science, 227, 1435 (1985)). To further assist the artisan, Table 1 (a and b) appearing on page 14 (original specification designation) specifically describes the "position corresponding" to the mutation points recited in Claim 2 for the alkaline proteases of SEQ ID NOs:2-7.

Therefore, the present claims do clearly allow the skilled artisan to recognize what has been invented and what is claimed is adequately described (including a sufficient number of representative species) in the specification within the meaning of 35 U.S.C. § 112, first paragraph.

Accordingly, withdrawal of this ground of rejection is requested.

The rejection of Claims 1, 2, 10, and 15 under 35 U.S.C. § 112, first paragraph ("enablement") is obviated in part by amendment and traversed in part.

The Office has taken the position that the claimed invention is not supported by an enabling disclosure (paper number 15, paragraph bridging pages 7 and 8). Applicants respectfully disagree.

At the outset, Applicants have amended Claim 1 to define the parent sequence as being SEQ ID NO:1, which the Examiner has conceded as being fully enabled. Therefore, the Examiner has already conceded compliance with the enablement requirement for this claim and the claims dependent therefrom.

Based on the Examiner's statement in support of rejection, it appears that the Examiner has based this ground of rejection on the difficulties associated with predicting structure and activity of a protein that is 60% homologous to the sequence of SEQ ID NO:1. Applicants believe that this rejection is obviated by the amendment present herein, in which Claim 2 and the claims dependent therefrom have amended to limit the scope of the claimed homologs to 80% of SEQ ID NO:1 for the regions outside of the claimed, alternative, mutation sites and to specifically require that the alkaline proteases within the scope of this claim have oxidant resistance, are active at an alkaline pH, and retain at least 80% residual activity when treated at pH 10 for 10 minutes.

MPEP §2164.04 states:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

On pages 5-8 (original specification designation), Applicants provide a detailed description of amino acid sequences that fall within the scope of the claimed invention. On page 8, line 13 to page 9, line 13 (original specification designation), Applicants provide 7

examples (SEQ ID NOs: 1-7) of alkaline proteases that may serves as the parent sequence. Moreover, with respect to the phrase "a position corresponding thereto," the Examiner's attention is directed to the specification at page 9, line 14 to page 13, line 20 (original specification designation). In this section of the specification the artisan is explicitly directed as to how one would identify the position corresponding to the claimed mutation points by use of the Lipman-Pearson method (Science, 227, 1435 (1985)). To further assist the artisan, Table 1 (a and b) appearing on page 14 (original specification designation) specifically describes the "position corresponding" to the mutation points recited in Claim 2 for the alkaline proteases of SEQ ID NOs:2-7.

MPEP § 2164.01 states:

> The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

Applicants submit that determining what sequences fall within or without the scope of the present claims would be readily apparent to the skilled artisan with the present application in hand. At page 15, line 1 to page 7 line 1 (original specification designation), Applicants provide a detailed description of how the skilled artisan may clone and express any variant. Moreover, at page 21, line 21 to page 31, line 13 (original specification designation), Applicants provide a detailed example of how the skilled artisan may clone, express, and characterize any sequence variant to assess its standing with respect to the claimed invention.

The Examiner has provided a rather nice account of some of the difficulties associated with predicting activity from sequence and structure. However, this discourse further underscores the fact that the activity now recited in these claims provides sufficient direction with respect to the scope of these claims, as well as the importance of the disclosure of the

present invention to provide the skilled artisan with express guidance to assess alkaline protease activity.

Applicants further note that the Examiner appears to have confused the standard of "quantity" of experimentation with "undue" experimentation. MPEP §2164.06 states:

> ... quantity of experimentation needed to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." In re Colianni, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Applicants submit that, with the present specification in hand, determination of polynucleotide sequences that fall within the scope of the present invention would require nothing more than routine experimentation to determine sequence homology and protein activity. As such, Applicants submit that the claims of the present application are fully enabled within the context of 35 U.S.C. §112, first paragraph.

Based on the foregoing, Applicants submit that the present claims are fully enabled by the specification and the common knowledge available in the art and as such withdrawal of this ground of rejection is requested.

The rejections of Claims 1, 2, 10, and 15 under 35 U.S.C. §102(b) over Hitomi et al, Tobe et al, and Christianson et al are obviated by amendment.

The present invention provides, in part, an alkaline protease that has oxidant resistance, is active at an alkaline pH, retains at least 80% residual activity when treated at pH 10 for 10 minutes, has an amino acid sequence which is at least 80% homology to the amino

acid sequence represented by SEQ ID NO:1, and has one or more amino acid residues selected from the group consisting of (a) position 84, (b) position 104, (c) position 256, and (d) position 369 of SEQ ID NO:1 or at a position corresponding thereto that has been specifically mutated to replace the original amino acid with an amino acid as follows:

at position (a): an arginine residue,

at position (b): a proline residue,

at position (c): an alanine, serine, glutamine, valine, leucine, asparagine, glutamic acid or aspartic acid residue, and

at position (d): an asparagine residue. (See Claim 2) Claim 1 further defines the parent sequence of the claimed alkaline protease as being that of SEQ ID NO: 1.

Applicants note that none of the art of record discloses the claimed alkaline protease. In particular, it is noted that each of Hitomi et al, Tobe et al, and Christianson et al disclose alkaline proteases in which the position corresponding to 369 is an aspartic acid. As presently claimed, the position corresponding to 369 has been mutated to be an asparagine residue.

In order for a reference to anticipate an invention, the reference "must teach every element of the claim" (MPEP §2131). Accordingly, in view of the failure by Hitomi et al, Tobe et al, and Christianson et al to specifically disclose or suggest an amino acid sequence in which the position corresponding to 369 has been mutated to be an aspartic acid would necessarily make this reference fail to anticipate the present invention.

Moreover, Applicants also note that Hitomi et al, Tobe et al, and Christianson et al fail to disclose or suggest any of the claimed mutations as positions (a) – (c). Therefore, these reference fail to anticipate the claimed invention, even after the Examiner expands the scope of the search to include the next species within the elected Group.

Applicants request withdrawal of the rejection of Claims 1, 2, 10, and 15 over Hitomi et al, Tobe et al, and Christianson et al.

The objection to Claim 1 is obviated by amendment. Applicants wish to thank the Examiner for bringing the typographical omission of a period to their attention. Withdrawal of this ground of objection is requested.

The objection to the Abstract is obviated in part by the submission of a substitute Abstract and traversed in part.

The Examiner has objected to the term "detergency" since it was not found in either the Random House College Dictionary, Steadman's Medical Dictionary, or the Oxford Dictionary of Biochemistry and Molecular Biology. However, the Examiner, as well as the skilled artisan, needs to look no further than the specification at page 29, line 7 to page 30, line 5 where "detergency" is defined as:

$$\text{Detergency (\%)} = \frac{\text{Brightness of the test fabric after washing} - \text{that before washing}}{\text{Brightness of the test fabric before soiling} - \text{that before washing}} \times 100$$

Moreover, this section provides an explicit description of how detergency is measured including each of the terms present in the above equation. Accordingly, the observation that "detergency" is not found in the cited references is of no moment as the definition of the term can be found within the four corners of the application. As such, the meaning of this term is clear and no further amendment is necessary.

For the Office's convenience, the substitute Abstract has been incorporated into the substitute specification (submitted herewith) as new page 42.

Applicants request acknowledgement that this objection has been withdrawn.

In addition, the objections to the specification and to the Figure Legend are obviated by submission of the attached substitute specification and substitute drawings. Applicants submit that the substitute specification contains no new matter. An indication that the objections to the specification and to the Figure Legend have been withdrawn is requested.

Finally, Applicants note the Examiner's indication that copending application Serial No. 10/385,662 may recite the same or overlapping inventions (paper number 15, page 6). The Examiner further notes that copending application Serial No. 10/385,662 is not available for review and, therefore, no determination has been made as to whether or not a double patenting situation exists. As such, the Examiner concludes: "If, upon availability of the above application to the Examiner, it is determined that there are conflicting claims between 10/385,662 and the instant application, double patenting will not be considered as new ground(s) of rejection." (paper number 15, page 6).

However, Applicants note that the claims of copending application Serial No. 10/385,662 were filed on May 27, 2003 and acknowledgment that this application was considered was provided with the Office Action mailed on August 12, 2003 (a copy of which is **enclosed herewith**). Accordingly, the Examiner was in possession of the original claims of 10/385,662 and has determined that no double patenting exists. Therefore, any change to this position would surely constitute a new ground of rejection. Moreover, if it is the Examiner's position that the claims are not rejected under all valid grounds due to the Office's unfortunate inability to timely provide the Examiner with copending application Serial No. 10/385,662, then it is noted that impermissible piecemeal examination is underway

(MPEP §707.07(g)). Again, it is clear that any rejection based on later availability of copending application Serial No. 10/385,662 would necessarily be a new ground of rejection.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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LIST OF RELATED CASES

Docket Number	Serial or Patent Number	Filing or Issue Date	Inventor/ Applicant
215483US0*	09/985,689	11/05/01	HATADA, et al.
234938US0	10/385,662	03/12/03	OKUDA, et al.

7/30/2003

*Present Application; listed for information